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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,091	07/15/2003	Steve Roffler	4910-2DIV2	8710

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,091	ROFFLER ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-25,27-33 and 35-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25,27-33 and 35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to the Amendment

The Amendment filed on 12/01/2005 in response to the previous Non-Final Office Action (08/30/2005) is acknowledged and has been entered.

Claims 21-25, 27-33 and 35-39 are currently pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-25, 27-33 and 35-37 **remain** and **new** claims 38-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of polyethylene glycol-containing compounds, which are cleared by an anti-polyethylene glycol antibody, and a genus of polyethylene glycol-containing conjugates comprising a tumor targeting means and a means for activating a genus of anti-tumor prodrug used for treating a tumor. However, the written description in this case only sets forth a polyethylene glycol-containing compound consisting of a PEG-modified βG which may be further covalently linked to a $F(ab')_2$ fragment of mAb B72.3 or mAb H25 and one species of polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a $F(ab')_2$ fragment of mAb B72.3 covalently linked to a PEG-modified βG which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of glucuranoid derivative of p-hydroxyaniline mustard.

The specification teaches (page 8, lines 11-13) that specific polyethylene glycol-containing compounds of the invention include, but are not limited to, compounds which are cleared from the circulation by an antibody against PEG with out significant toxic side effects. The specification further teaches (page 8, lines 9-11 and page 9, lines 7-9) the development of PEG-modified compounds which are useful in cancer therapy, wherein the PEG-containing compound comprises a tumor targeting means and a means for activating an anti-tumor prodrug to the patient. Although the specification (page 19) discloses the accelerated clearance of two polyethylene glycol containing compounds comprising a PEG-modified βG covalently linked to mAb's B72.3 or H25, the written description (page 43, lines 3+) only appears to reasonably convey one species polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a $F(ab')_2$ fragment of mAb B72.3 covalently linked to a PEG-modified βG which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of a glucuranoid derivative of p-hydroxyaniline mustard. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of compounds that encompass the genus of polyethylene glycol-containing compound which are rapidly cleared from blood circulation by administration of an anti-polyethylene glycol antibody nor does it provide a description of structural features that are common to the compounds. Further, the specification fails to provide a representative number of conjugates that encompass the genus of polyethylene glycol-containing conjugates comprising a tumor targeting means and a means for activating a genus of anti-tumor prodrug used for treating a

tumor nor does it provide a description of structural features that are common to the conjugates. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of two species of polyethylene glycol-containing compounds, which are cleared by an anti-polyethylene glycol antibody and one species of polyethylene glycol-containing conjugates comprising one tumor targeting means and one means for activating a single anti-tumor prodrug used for treating a tumor is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of polyethylene-gylcol containing compounds and conjugates, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only two species of polyethylene glycol-containing compound consisting of a PEG-modified βG which may be further covalently linked to a $F(ab')_2$ fragment of mAb B72.3 or mAb H25 and one species of polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a $F(ab')_2$ fragment of mAb B72.3 covalently linked to a PEG-modified βG which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of glucuranoid derivative of p-hydroxyaniline mustard, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-*

Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In response to this rejection, Applicants contend that the present invention is directed to using an anti-polyethylene glycol (PEG) antibody to remove PEG-containing compounds in the blood circulation. As such, Applicants assert that the common structural feature of these PEG-containing compounds is PEG which is the only potion in the PEG-containing compounds relevant to the present invention because the antibody is specific to PEG. Normally, Applicants submit that this antigen (PEG) and antibody relationship will not be altered by the nature of other parts of a PEG-containing compound. Therefore, a person of ordinary skill in the art would expect that the antibody binds one PEG-containing compound will bind the other as well. Moreover, Applicants argue that the written description requirement only requires a patentee to sufficiently describe the invention and not every detail unrelated to the invention. Hence, Applicants contend that the invention is to use an anti-PEG antibody to remove PEG-containing compounds in the blood circulation, not the compound per se. Furthermore, Applicants assert that it is unnecessary to describe other PEG-containing compounds as the PEG portions of all such compounds are the same and can be logically concluded that those other PEG-containing compounds can be removed in the same manner based on the common knowledge about antibody-antigen reaction.

These arguments have been carefully considered, but are not found persuasive.

In response to Applicants contention that the present invention is directed to using an anti-polyethylene glycol (PEG) antibody to remove PEG-containing compounds in the blood circulation, wherein the common structural feature of these PEG-containing compounds is the PEG, the Examiner acknowledges that the present invention is directed to the removal of PEG-containing compounds in the blood circulation using an anti-PEG antibody. However, the Examiner recognizes that while the structural feature common to the genus of PEG containing compounds is indeed PEG, a lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA

1967). In this case, as stated above, the written description (page 43, lines 3+) only appears to reasonably convey one species polyethylene glycol-conjugates used for the treatment of a tumor, wherein the tumor targeting "agent" is a $F(ab')_2$ fragment of mAb B72.3 covalently linked to a PEG-modified βG which activates one species of prodrug referred to as the tetra n-butyl ammonium salt of a glucuranoid derivative of p-hydroxyaniline mustard. In response to Applicants assertion that the invention is to use an anti-PEG antibody to remove PEG-containing compounds in the blood circulation, not the compound per se, the Examiner acknowledges that the claims are directed to the use of an anti-PEG antibody. However, the Examiner recognizes that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). As such, while the specification teaches one of ordinary skill in the how to use the invention, the specification does not reasonably convey that they were in possession of the genus of polyethylene glycol-containing compounds.

New Objections necessitated by Amendment.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter in claims 38 and 39. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

For each deposit made pursuant to the regulations for Deposit of Biological Material set forth in MPEP 1801, the specification shall contain:

(1) The accession number for the deposit;

(2) The date of the deposit;

(3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and

(4) The name and address of the depository.

Therefore, No claim is allowed.

In the instant case, the claims appear to be free of the prior art. The closes prior art which teaches the instantly claimed method appears to be Griffiths et al. (US 6,077,499, 2000, of record) which teaches a method of treating a tumor comprising administering a first conjugate, which contains a tumor targeting moiety, a therapeutic agent, and a fist member of a binding pair; followed by administration of a clearing agent which contains the complementary biding member or the binding pair and a second therapeutic agent such as a prodrug. However, Griffiths et al. does not teach the clearing agent is a antibody to polyethylene glycol and there does not appear to be any suggestion or motivation in the prior art to combine the two.

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
3/17/06